

CLAIMS

1. A method for regulating expression of a *tet* operator-linked gene in a cell of a subject, comprising:
 - 5 introducing into the cell a nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject.
- 10 2. The method of claim 1, wherein the Tet repressor of the tTA is a Tn10-derived Tet repressor.
- 15 3. The method of claim 1, wherein the polypeptide of the tTA which directly or indirectly activates transcription in eucaryotic cells is from herpes simplex virus virion protein 16.
- 20 4. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is integrated randomly in a chromosome of the cell.
- 25 5. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is integrated at a predetermined location within a chromosome of the cell.
6. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is introduced into the cell *ex vivo*, the method further comprising administering the cell to the subject.
7. The method of claim 1, wherein the *tet* operator-linked gene is an endogenous gene of the cell which has been operatively linked to the at least one *tet* operator sequence.
- 30 8. The method of claim 1, wherein the *tet* operator-linked gene is an exogenous gene which has been introduced into the cells.
9. The method of claim 1, wherein the tetracycline analogue is anhydrotetracycline, doxycycline or cyanotetracycline.
- 35 10. A method for regulating expression of a gene in a cell of a subject, comprising:
 - obtaining the cell from the subject;
 - introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one *tet* operator sequence;

introducing into the cell a second nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells, to form a modified cell;

- 5 administering the modified cell to the subject; and
modulating the concentration of a tetracycline, or analogue thereof, in the subject.

11. The method of claim 10, wherein the Tet repressor of the tTA is a Tn10-derived Tet repressor.

- 10 12. The method of claim 10, wherein the polypeptide of the tTA which directly or indirectly activates transcription in eucaryotic cells is from herpes simplex virus virion protein 16.

- 15 13. The method of claim 10, wherein the nucleic acid molecule encoding the tTA is integrated randomly in a chromosome of the cell.

14. The method of claim 10, wherein the nucleic acid molecule encoding the tTA is integrated by homologous recombination at a predetermined location within a chromosome
20 of the cell.

15. The method of claim 10, wherein the first nucleic acid molecule operatively links an endogenous gene of the cell to at least one *tet* operator sequence.

- 25 16. The method of claim 10, wherein the first nucleic acid molecule comprises a gene operatively linked to at least one *tet* operator sequence.

17. The method of claim 10, wherein the tetracycline analogue is anhydrotetracycline, doxycycline or cyanotetracycline.